COMPARATIVE STUDY OF LEFT VENTRICULAR FUNCTION BY ECHOCARDIOGRAPHY IN TYPE 2 DIABETES MELLITUS PATIENTS WITH AND WITHOUT RETINOPATHY

DISSERTATION SUBMITTED TO
THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the regulations
For the award of the degree of

M.D. BRANCH I
GENERAL MEDICINE

GOVT. STANLEY MEDICAL COLLEGE AND HOSPITAL, CHENNAI - 01

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY CHENNAI

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CERTIFICATE

This is to certify that this dissertation titled **"COMPARATIVE STUDY OF LEFT VENTRICULAR FUNCTION BY ECHOCARDIOGRAPHY IN TYPE 2 DIABETES MELLITUS PATIENTS WITH AND WITHOUT RETINOPATHY"** is the bonafide original work of **DR.BHARGAVI. K**. in partial fulfillment of the requirements for M.D. Branch-I - General Medicine examination of The TamilNadu Dr. M. G. R. Medical University to be held in April 2013. The period of study was from March 2012-October 2012.

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DECLARATION

I, Dr. BHARGAVI.K., solemnly declare that this dissertation titled **"COMPARATIVE STUDY OF LEFT VENTRICULAR FUNCTION BY ECHOCARDIOGRAPHY IN TYPE 2 DIABETES MELLITUS PATIENTS WITH AND WITHOUT RETINOPATHY"** is a bonafide work done by me in the Department of General Medicine, Government Stanley Medical College & Hospital during the period of March 2012 to October 2012 under the guidance and supervision of **Prof. Dr. G. SUNDARAMURTHY, M.D.,** Professor of Medicine, Govt. Stanley Medical College & Hospital, Chennai-1. I also declare that this bonafide work or a part of this work was not submitted by me for any award, degree, diploma to any other university, board either in India or abroad.

This dissertation is submitted to The Tamil Nadu Dr. M. G. R. Medical University, Chennai towards partial fulfillment of requirement for the award of M. D. Degree Branch-I in General Medicine.

Place: Chennai,
Date :

Dr. Bhargavi. K.

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CONTENTS

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INTRODUCTION

Diabetes mellitus is a disease whose incidence is increasing worldwide and gaining epidemic proportions. Among all its complications, cardiovascular disease is in majority, the frequent reason for mortality (1).

Over the last 30 yrs, numerous statistical, clinical and post-mortem studies have identified diabetic cardiac disease to be a separate clinical variable. (2-5). Numerous studies have shown diabetes can affect the structure as well as functions of the heart even without conventional threat factors such as coronary artery disease and hypertension.

Diabetic cardiomyopathy has been advocated as an independent cardiovascular disease and multiple mechanisms such as microvascular pathology, autonomic dysfunction, disorders in metabolic pathways and interstitial fibrosis have been proposed as causative factors (6).

However, the accurate aetiopathogenesis of diabetic cardiomyopathy is not clear. New studies prove that diseases involving

both the microvasculature and macrovasculature are associated with coronary events.

Diabetic cardiomyopathy is characterised by defects in functions of both systole and diastole (7). Diabetic heart disease's spectrum progresses from being normal to preclinical dysfunction of diastole and systole, leading to overt echocardiographic indices of evident LV dysfunction and ultimately fully blown heart failure with symptoms. In patients sans overt disease at beginning, the occurrence of subclinical ailment has association with augmented risk of cardiac disease,(8) with the amplified risk of overall death as 3 for men and 1.7 in women (9). Apart from the mortality, there is impairment of functional capacity as well.

After the onset of full blown heart failure signs and symptoms the prognostic prospects are generally worse (10-13). Hence, measures to identify risk variables contributing to this burdensome cardiac failure in subjects of diabetes mellitus are crucial in decreasing the associated moribund status.

Current statistics from the study of Atherosclerosis Risk in Communities (ARIC) has exhibited a connection involving retinopathy,

and heart failure development (14). The former is a microvascular disease indicator and the latter is traditionally viewed as a macrovascular disease. With more worsening of retinopathy severity, the mass of left ventricles increased, so also that of atrium and the systolic fraction decreased. These findings were found independent of influential confounding variables.

Another study namely the Multi-Ethnic Study of Atherosclerossis (MESA) also established that retinopathy was coupled with accelerated remodeling of cardiac structures as evidenced by MRI of the heart in diabetic patients (15).

Thus the studies lead to a possible suggestion that there exists a probable microvascular involvement in the concurrence of cardiac dysfunction coupled with diabetes or a potential link between microvascular retinopathy and the so called macrovascular heart disease due to common pathophysiological pathways of both disorders (16-18).

In an era where both diabetes and heart failure contribute to the overall burden of the medical system, it is prudent to identify abnormalities contributing to the linked association between heart failure and retinopathy. At least, we should trigger evaluation of retinopathy in

type 2 diabetes patients for further cardiac status. And further treatments targeted at the microvascular disease may ultimately decrease macrovascular disease risk as well and that might be greatly beneficial in the vast diabetic population.

REVIEW OF LITERATURE

HISTORY

Diabetes mellitus is one of the foremost diseases to be described, with an Egyptian manuscript as early as 1500 B.C. where it is mentioned as TOO GREAT EMPTYING OF THE URINE.

The first complete clinical description of diabetes was given by a physician of Greece by name Aretaeus from Cappadocia. He also coined the name “diabetes.” Thomas Willis of England in 1675 later added the word mellitus meaning honey/sweet.

Indian physicians Sushruta and Charaka identified separately types 1 and 2 diabetes in 400-500 AD. Sir Harold Percivial Himsworth clearly made the distinction in 1936.

The role of the liver in glycogenesis was established by French physician Claude Bernard in 1857.

The contribution of pancreas in causing diabetes was identified by Mering and Minkowski belonging to Austria.

An important milestone was the discovery of insulin by Canadians - Banting and Best in 1921. Oral Hypoglycemic Agents were subsequently discovered and marketed in 1955.

BANTING AND BEST

CLASSIFICATION ACCORDING TO ETIOLOGY:

1) Type 1 DM

   A. Immune-regulated

   B. Idiopathic

2) Type 2 DM

3) Additional definite forms

   A. Genetic problems of function of beta cells due to mutations:

      1. Maturity Onset Diabetes in Young - MODY 6 types

      2. Mitochondrial DNA

      3. Involving ATP K+ channel

      4. Insulin/Proinsulin

   B. Genetic derangements in action of insulin

      1. Insulin resistance-Type A

      2. Leprechaunism

      3. Lipodystrophy

C. Pancreas – exocrine part diseases

D. Endocrinopathies

E. Drug- or chemical-induced

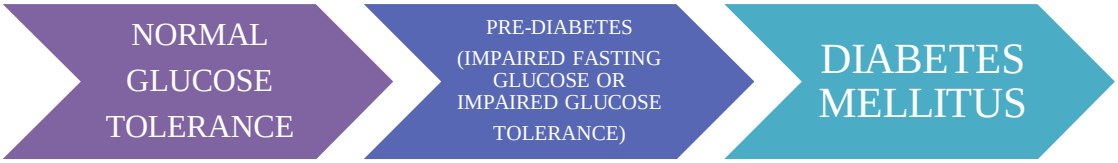
F. Viral Infections

G. Rare forms of immune-regulated diabetes

H. Genetic syndromes

4) Gestational DM

SPECTRUM OF DIABETES



DIAGNOSTIC CRITERIA:

As proposed by the AMERICAN DIABETES ASSOCIATION 2011,a diagnosis of DM is made by presence of either of the following:

- Diabetic symptoms + a random blood glucose of 200 mg/dl.
- Plasma glucose in fasting state of 126 mg/dl.
- 2 hr post prandial plasma glucose of 200 mg/dl.
- HbA1C >6.5%

RISK ATTRIBUTES

Family history

Obesity

Lack of activity

Specific ethnicity

History of GDM

High blood pressure

Low HDL cholesterol level or high triglycerides

PCOS or Acanthosis nigricans

Post cardiac disease

COMPLICATIONS

ACUTE COMPLICATIONS

The acute complications are ketoacidosis and nonketotic hyperglycemic hyperosmolar coma. Though the latter is seen predominantly in type 2 DM, DKA is no more considered pathognomonic of type 1 DM as it can occur with either types. The characteristics are depletion of volume, abnormalities of acid-base and absolute or relative deficiencies of insulin with or without ketosis.

CHRONIC COMPLICATIONS

It affects multiple organ systems contributing to majority of morbidity and mortality.

VASCULAR	
MICROVASCULAR	**MACROVASCULAR**
Retinopathy	Cardiovascular system disease
Neuropathy	Peripheral vascular disease
Nephropathy	Stroke

NON-VASCULAR
Altered bowel habits
Urogenital problems
Skin diseases
Susceptibility to infections
Eye - glaucoma, cataracts
Periodontal disease
Loss of Hearing

The risk of incurring the above complications amplifies with the time duration and severity. But since the type 2 disease has a lengthy symptomless period, many patients present with complications even initially during diagnosis.

COMPLICATIONS INVOLVING THE MICROVASCULATURE:

RETINOPATHY

It is among the foremost microvascular complications in DM. It is characterized by typical lesions involving the microvasculature of the retina such as microaneurysms, haemorrhages and exudates. The others are venous changes, neovascularisation and thickening of the retina. Ultimately if left untreated, it might lead to loss of vision.

NEPHROPATHY

It is a severe complication which has the hallmark features of thickened basement membranes, glomerular hyperfiltration, expansion of mesangium and matrix, formation of Kimmelsteil-Wilson nodules and glomerular and tubular sclerosis .The earliest manifestation is

microalbuminuria, which progresses to frank albuminuria and eventually to renal failure and end-stage renal disease (ESRD) (19-22).

DIABETIC NEUROPATHY

Peripheral neuropathy manifests as various forms such as sensory, motor-focal/multifocal and autonomic neuropathies. The most common form is chronic sensorimotor distal symmetric polyneuropathy. Pure sensory neuropathy is quite rare. Mononeuropathies occur with the nerves of the upper limb-median nerve, ulnar or the radial nerve or even the cranial nerves.

Diabetic amyotrophy is a condition where there is pain, weakness of muscles and hypotrophy involving the muscles of thigh. All these may ultimately lead to foot injury, ulceration and, amputations. Autonomic neuropathy manifests by gastroparesis, constipation, diarrhoea, sexual and bladder dysfunction, intolerance of exercise, tachycardia at rest and sudden cardiac death.

MACROVASCULAR COMPLICATIONS:

CARDIAC DISEASE

It is the chief cause of mortality in diabetic people who have 4.5 times increased danger for cardiac disease even after adjusting for conventional risk attributes such as high BMI, altered lipid profile and high BP. These attributes combined with the sole independent attribute of diabetes per se notably augment risk for cardiovascular disease.

CEREBROVASCULAR DISEASE

Diabetes mellitus is an autonomous risk variable in every age group for cerebrovascular disease; so also for severe neurological deficits and the following disability and also for sudden death. Risk factors are hyperglycemia, atrial fibrillation and also the microvascular complications.

PERIPHERAL VASCULAR DISEASE

It is manifested by arterial occlusion of legs, leading to claudication and pain intermittently and chiefly upon stress. Hyperglycemia, obesity, high serum fibrinogen levels and physical

inactivity contribute to it. The central pathogenesis is atherosclerosis. Other contributors are increased tendencies for platelet adhesion, aggregation, therefore hypercoagulable state and impaired fibrinolysis (28-32).

CURRENT LITERATURE OF THIS STUDY

The recognition of a cardiomyopathy in diabetics was primarily projected by Rubler et al on the background of autopsy results (33). Both systolic and diastolic function abnormalities have been established in studies done in humans as well as in animals (34-37). The etiology of this type of LV dysfunction is not totally known (38).

Studies done in DM without CAD have verified that in people with various grades of retinopathy, dysfunction in diastole was present compared to people without retinopathy (39, 40). In a study by Annonu et al, a greater frequency of retinopathy was noted in subjects with atypical LV filling compared to the standards with normal diastole (41).

Nevertheless, this link was not persistently found. In the analysis by Airaksinen et al (42) and Uusitupa et al(43) , retinopathic patients did not diverge from the other subjects.

DIABETIC RETINOPATHY

INTRODUCTION

A major microvascular complication of diabetes is diabetic retinopathy. It occurs in both the types and it has been observed that virtually all type 1 and 76 % of DM will go on to retinopathy after 15 yrs (44). In our country with the drastic surge in type 2 DM, diabetic retinopathy has become a chief cause of visual disability (45).

Nevertheless, this is hugely avertable and manageable with timely intervention.

RISK FACTORS

Apart from the ocular factors like detachment of the vitreous, surgeries for cataract and chorioretinopathies, various systemic factors also play a role in the pathogenesis of diabetic retinopathy.

SYSTEMIC FACTORS
Gender
Diabetic duration
Control of glycemic status
High BP
Renal disease
Dyslipidemia
Alcohol
Anemia
Obesity

SEX: Various analyses have failed to show stable outcomes in evaluating gender as a risk variable in retinopathy.

DISEASE DURATION: The time duration of diabetes disease is perhaps the most important risk variable for developing retinopathy. This

goes with the studies of WESDR (44), Dandona et al (46) and CURES Eye study (47) .Furthermore it has also been studied that for each 5 year increase in span of disease, retinopathy risk is amplified by 2 .

CONTROL OF GLYCAEMIC STATUS: This fact that glycemic levels reflect on retinopathy is supported by studies like WESDR, DCCT and UKPDS (44, 48, 49).

HYPERTENSION: Studies have proven association betweeen high BP and the concurrence and severity of retinopathy in diabetic population (49, 50).

RENAL DISEASE: The links between angiopathy in renal and retinal systems in diabetes have been studied (51, 52). These may possibly be mediated through hypertension, high levels of fibrinogen and altered lipoproteins.

DYSLIPIDEMIA: This may contribute in the form of increased total serum cholesterol, elevated fractions of low-density form or triglycerides (44, 53).

ALCOHOL: Young *et al* and The Casteldaccia Eye Study (54, 55) have linked alcohol and retinopathy with respect to quantity and duration of alcohol. But this is disproved in WESDR (44).

OBESITY: BMI had a noteworthy value in retinopathy as evidenced by CURES (47), Zhang et al.(56)

OTHER FACTORS

- increased oxidative stress (57)
- Growth factors such as VEGF,GH and TGF- β
- intima-media thickness and arterial stiffness
- decreased glutathione levels
- genetic factors

MOLECULAR PATHOGENESIS OF RETINOPATHY

The range of changes that could occur in the retina are:

(*i*) Development of capillary microaneurysms

(*ii*) Undue vascular permeability

(*iii*) Vascular occlusion

(*iv*) Angiogenesis and new fibrous tissue formation.

(*v*) The tightening of the above fibrovascular proliferations (58).

Four key biochemical pathways are in proposal (59). They are:

(*i*) Improved glucose flux via the polyol gateway.

(*ii*) Augmented production of advanced glycation end-products

(*iii*) Protein kinase C activation.

(*iv*) Activation of hexosamine gateway.

GRADING

1) BACKGROUND (NON-PROLIFERATIVE) DIABETIC RETINOPATHY:

It is defined by occurrence of microaneurysms, intraretinal hemorrhages which could be punctuate or striate and exudates, particularly hard exudates. Microaneurysms are tiny vascular outpouchings occuring as the earliest finding. They seem as red dots on visualisation of the retina.

Haemorrhages are classically of the dot type. Hard exudates are formed due to accumulation of lipid over the edges of hemorrhages. Edema of the retina may be due to microvascular leakage as a result of breach of blood retina barrier.

Fig-1. Background diabetic retinopathy

2) PREPROLIFERATIVE type is described by exudates (soft), venous beading, and intraretinal microvascular abnormalities.

Fig- 2. Preproliferative diabetic retinopathy

3) PROLIFERATIVE DIABETIC RETINOPATHY depicted by neovascularization on disc or contained by one disc diameter from the disc. The former is known as new vessels on the disc (NVD) and the latter is known as new vessels elsewhere (NVE).

Fig -3. Proliferative diabetic retinopathy with NVD.

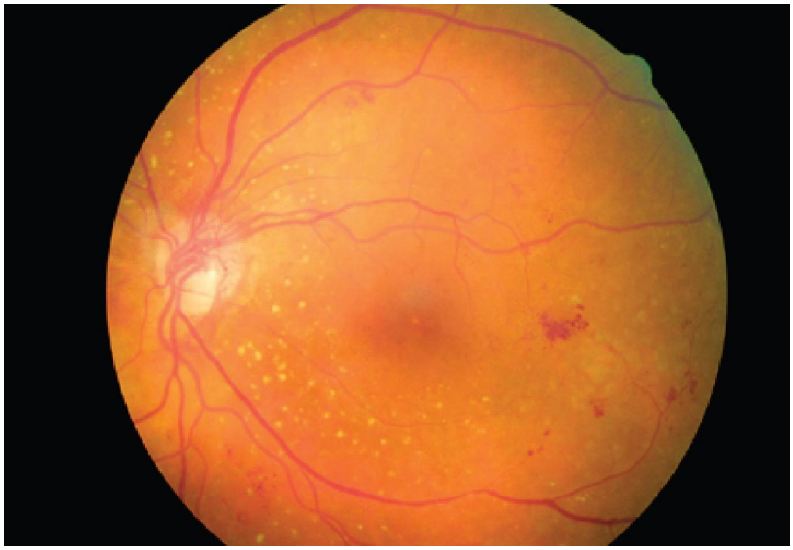


Fig-4. Proliferative type with haemorrhages in vitreous and pre-retinal zone.

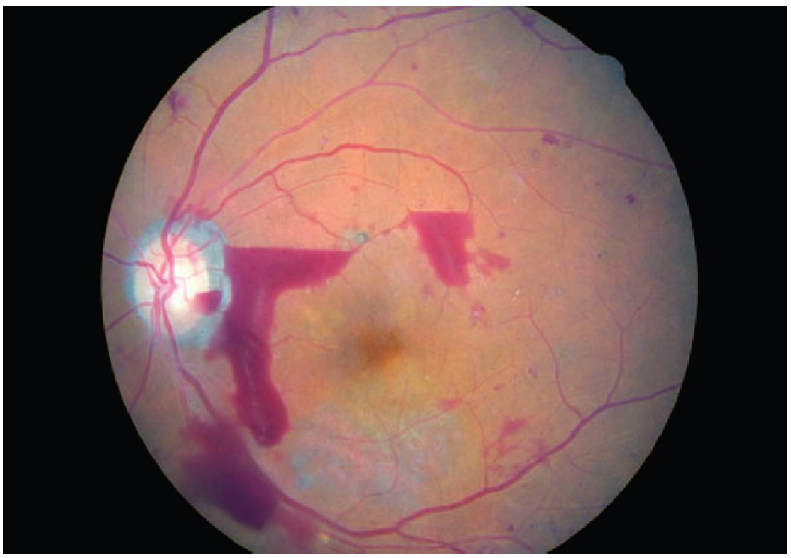
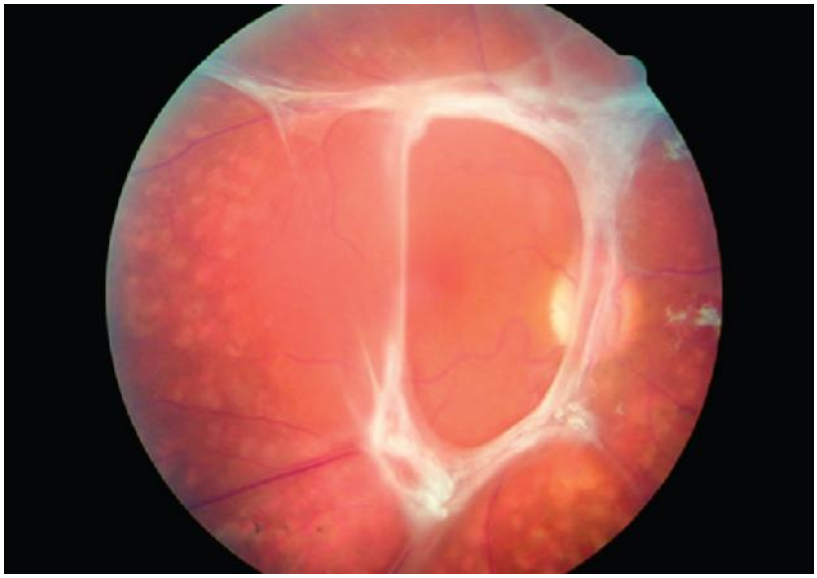


Fig-5. Proliferation of fibrous tissue

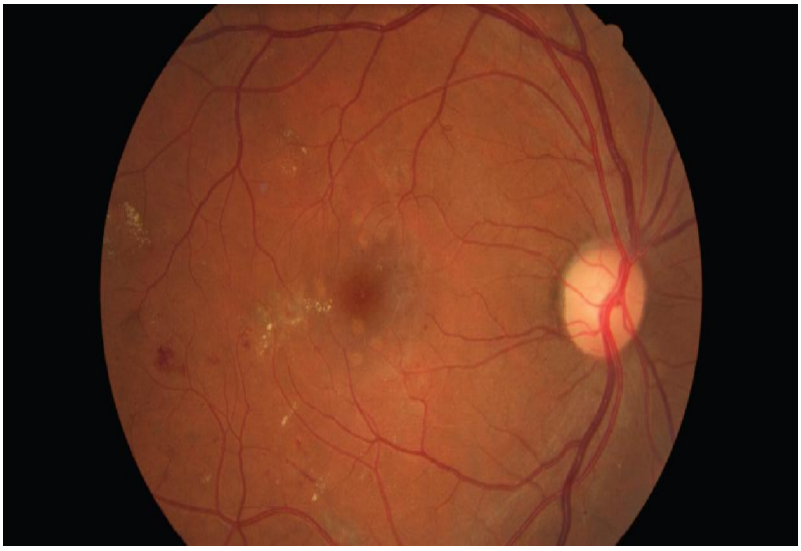


All these can ultimately lead to vitreous hemorrhage, traction detachment of retina and finally blindness.

4) **DIABETIC MACULAR OEDEMA**

It is defined as edema manifesting as thickening encircling within two disc diameters from the macular centre. If quite close to the centre of macula, it is known as clinically significant macular edema (CSME).

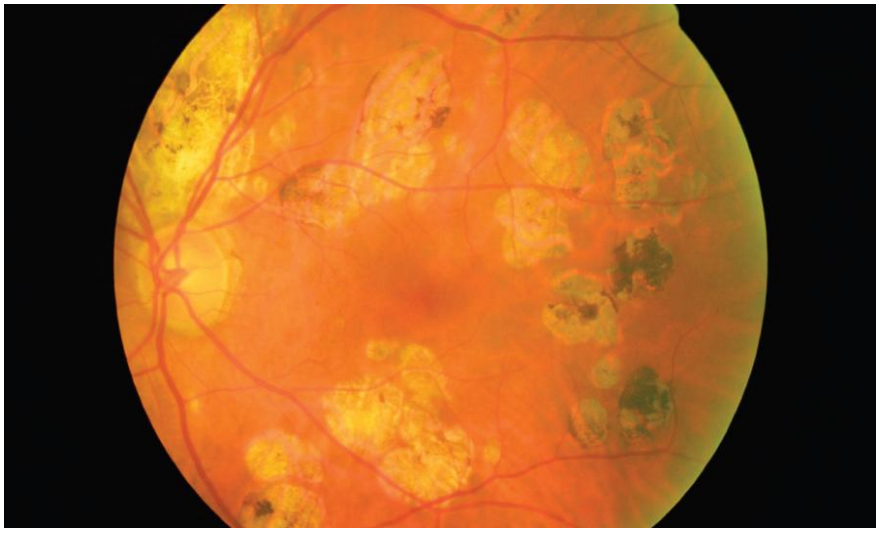
Fig-6. Diabetic Maculopathy



5) POST PHOTOCOAGULATION STATUS

This type is one where there are multiple small scars in the retinal periphery as a result of photocoagulation**.**

Fig-7. Retinal view after photocoagulation.



6) UNCLASSIFIABLE

This type of retinopathy is ungradeable, probably because of difficulty in visualization because of opacities like cataract.

DIAGNOSIS AND MANAGEMENT

Diagnosis depends on the appearance and evolution of DR and on the factors that influence this.

The retina is usually studied by

- Ophthalmoscopy
- Slit lamp Biomicroscopy
- Fundus photography (gold standard)
- Digital colour photography
- Optical coherence tomography (OCT).

Management strategies are Laser photocoagulation and vitrectomy . Intravitreal injections of steroids may be useful in severe CSME. Few antiproliferative agents are also under trial.

DIABETIC LV DYSFUNCTION

Diabetic cardiomyopathy is a syndrome continuum that involves the myocardium and resulting in a number of derangements in structure ultimately leading to hypertrophy of left ventricle and abnormalities of systole or diastole or both. It is already known that diabetics are at increased risk of high BP and coronary artery disease (32); however diabetic cardiomyopathy can occur without the presence of these other factors.

Thus by definition, it is a “unique entity featured by abnormal myocardial function or structure in the lack of CAD / hypertension / valvular heart disease.”

FACTORS CONTRIBUTING:

AGE

It is a vital variable determining cardiovascular disease, whose incidence is appreciably higher in patients above the age of 60 years (26).

SEX

Diabetes is probably the only condition in which women have heart diseases rates equal to men. In the Rancho Bernardo Study diabetic women had ischemic heart disease mortality rates higher than men. This could be because of women's lipoprotein profile being altered when associated with diabetes. Still, though diabetes accelerates the virtual risk in females, the total danger for cardiac mortality is undoubtedly larger in males than females (25).

HYPERGLYCEMIA, DURATION OF DIABETES AND GLYCEMIC CONTROL

Hyperglycemia is a stronger interpreter of microvascular complication when compared to macrovasculart disease in diabetics. Unoptimally treated hyperglycemia is a potential risk attribute (24, 49). The associations between glycemic control and diastolic filling were found positively in studies of Hiramatsu (28), Vanninen (29) and Beljic et al (30). Holzmann studied the association of HbA1C and heart disease in individuals with Non insulin dependent diabetes (31).

HYPERTENSION

Elevated blood pressure levels have been noticed in diabetics quite consistently independent of age, BMI and renal disease and its prevalence accelerates with duration of diabetes and is greatly accentuated in the presence of diabetic nephropathy (60) .The mechanisms are not well understood, but possibly due to insulin and its actions.

DYSLIPIDEMIA

Hypertriglyceridemia, possibly due to more availability of free fatty acid and glucose to the liver leads to enormous production of VLDL; lipoprotein lipase's abnormal function results in poor clearance of both chylomicrons and VLDL. Elevation of total or LDL cholesterol and decreased HDL cholesterol are other contributors (61-63).

ALCOHOL

Both duration and quantity of alcohol consumption are influencers of cardiovascular disease. Generally alcoholic diabetics consuming > 90 g of alcohol a day for five years are at danger. Alcoholic cardiomyopathy, a

nonischemic type of dilated cardiomyopathy is depicted by an increase in mass of myocardium, ventricle dilatation and thinning of walls.

STROKE

Cerebrovascular accidents are the other major macrovascular complication of diabetes like cardiovascular disease. Whether they both are individual contributors to each other is a matter of debate.

MICROALBUMINURIA

Studies by Sampson et al (20) and Perez et al (21) demonstrated a decrease in E/A ratio in diabetics according to the presence of microalbuminuria. Albuminuria is currently shown in numerous studies to be a significant independent predictor of cardiovascular disease in diabetics (64-67). This further leads to the fact that association between diabetes and cardiovascular disease may have similar determinants with microvascular complication in the other organs as well.

CARDIOVASCULAR AUTONOMIC NEUROPATHY

It is manifested as tachycardia at rest, intolerance of exercise, perioperative cardiovascular instability, orthostatic hypotension, silent MI

and the Cardiac Denervation Syndrome, manifesting as abnormalities in LV systolic and notably diastolic function (68). This was demonstrated in studies of Monteagudo *et al* (22) and Sacre et al (69).

PERIPHERAL VASCULAR DISEASE

Patients might have an extraordinarily increased risk for cardiac events, particularly large-vessel disease (70). Its prognosis as correlated with the severity is calculated by the Ankle brachial index (71).

THYROID

Abnormalities in cardiac performance can occur in both patients with hyperthyroidism state or hypothyroidism parallel with diabetes. Contractility of the myocardium is augmented in the hyperthyroid and decreased in hypothyroidism. This is probably because of alterations in the proteins causing cardiac contraction. It is due to cumulative effects of the thyroid hormone per se and also changes in the cardiac responsiveness to sympathetic and hemodynamic alterations.

OTHER ENDOCRINE DISORDERS like adrenal cortical insufficiency and acromegaly also cause cardiovascular disease by a variety of causes.

CUMULATIVE RISK FACTORS

Type 2 diabetics usually have manifold heart disease risk factors, in the likes of hypertension, altered lipid profile, absence of activity, smoking and central obesity. Additive risk variables significantly multiply the all over cardiac risk (27).

OTHER FACTORS

The Insulin Resistance Syndrome (72), chronic inflammatory state, disturbed function of endothelium (73) and thrombotic state are all said to contribute to diabetic cardiac disease.

PATHOPHYSIOLOGY

The earliest finding is diastolic dysfunction, i.e., dysfunction of ventricular relaxation and passive filling. In cardiomyopathy with systolic failure, collagen deposition in myocardium (74) and AGE (75) are the chief pathological processes leading to loss of elasticity of the

myocardium, whereas augmented cardiomyocyte resting tension (76) could be the chief cause in diastolic failure.

Four main causes are responsible for this:

- Microangiopathy and thereby dysfunction of endothelium (73).
- Autonomic neuropathy.
- Alterations in metabolism such as altered glucose usage and augmented oxidation of fatty acid, production and accretion of free radicals.(77)
- Changes in ion dynamics, particularly calcium (78), decreased function of Na^{+}-Ca^{2+} swap pump systems, decrease in a Na^{+}-K^{+} ATPase subunit expression and other potassium current disturbances.

STRUCTURAL CHANGES

Changes in the structure are reflected by hypertrophy of the ventricle. LVH is usually stated as the upper five percentage of the distribution of LV mass in the general population and this could be assessed by ECG criteria or ECHO.

FUNCTIONAL ALTERATIONS

DYSFUNCTION OF SYSTOLE

It is an impaired ability of the heart to drive out blood; the chief feature of systolic dysfunction is a decreased LV ejection fraction. The various determinants found in the echo evaluation are:

1. Ejection fraction calculation by LV dimensional technique – Simpson's method or M- mode Echocardiography.

2. dP/dT of the regurgitant jet across the mitrals.

3. Doppler calculation of stroke volume and thence the total output.

DIASTOLIC DYSFUNCTION

Diastolic phase of the heart has 4 subphases namely (79)

- Relaxation-isovolumic phase,
- Premature filling,
- Diastasis,
- Contraction of atrium.

FACTORS INFLUENCING LV FILLING

- Relaxation of myocardium
- Contraction of atria
- Viscoelastic properties
- Pericardial influences
- Inter Ventricular interaction
- Turgor of Coronary arteries
- Pre- load and after load.
- Conduction pathway.

Their ultimate summated effect is over the transmitral gradient of pressure that decides filling of left ventricle (80). The reason for dysfunction of diastole may be further divided as a fall of compliance of the myocardium passively as well as impaired active LV relaxation.

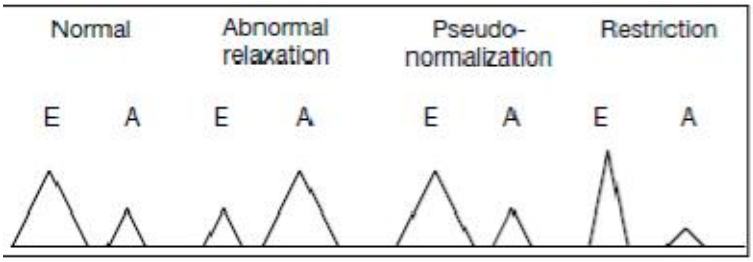
TECHNIQUES TO IDENTIFY DIASTOLIC DYSFUNCTION

Traditionally, cardiac catheterization with measurements of pressure and volume was the method of choice for evaluating diastolic function, which could manifest much earlier than systolic dysfunction (81, 82). The relaxation rate, rapidity and time span of filling and

stiffness of chambers can be determined but it is an invasive technique (83).

Of now, **DOPPLER ECHOCARDIOGRAPHY (**84,85) has become a vital and easy to do noninvasive diagnostic measure .The transmitral flow exhibits a biphasic pattern, with an early crest indicating swift early diastolic filling (peak E) and a delayed crest indicating contraction of atria (peak A). Based on this, a structure of grading is designed.

Three classical abnormal filling types typically on the basis of E/A ratio have been put forth (86).



1. The 1st type called “delayed relaxation”, leads to a reversal of E/A ratio (E/A ≤1) where relaxation is hampered.

2. The 2nd type, depicting dysfunction of relaxation and compliance, known as pseudonormalization, due to normalized E/A ratio (E/A

equaling 1). This is because left atrial pressure increases to compensate for slow relaxation.

3. The third type, known as “restrictive filling”, seen in extreme fall in ventricular compliance leading to a high E/A ratio (above 2).

TISSUE DOPPLER ECHOCARDIOGRAPHY

The advantage is that it is not influenced by changes in pre-load. It also identifies cardiac contraction both longitudinally and circumferentially, enabling it to detect even subtle dysfunction.

INTRAVENOUS CONTRAST ECHOCARDIOGRAPHY

It provides an assessment of integrity of the microvasculature and thus perfusion using the resonance of microbubble contrast agents.

3D ECHO

It does not use arithmetic predictions to quantify volumes on the contrary to 2D. It is of particular usefulness in ventricles with unusual shapes and regional wall motion abnormalities.

COMPUTED TOMOGRAPHY

The coronary artery calcification score can be calculated using but its significance with diabetic cardiomyopathy is not known.

MRI (MAGNETIC RESONANCE IMAGING)

MPI (myocardial perfusion imaging) and thence assess MFR (myocardial flow reserve) can be assessed using MRI.

SPECT (SINGLE PHOTON EMISSION CT)

It is an on-par system to nuclear cardiology for the identification of vessel abnormalities and myocardial perfusion.

MANAGEMENT

Diabetic cardiomyopathy requires multipronged treatment approach as the causes are multifactorial. It includes optimal glycemic control by way of diet modification, OHAs, insulin and treatment of failure symptoms. Angiotensin converting enzyme (ACE) inhibitors and beta blockers may be particularly useful in influencing ventricular remodeling.

ASSOCIATION BETWEEN DIABETIC RETINOPATHY AND LEFT VENTRICULAR DYSFUNCTION

Researchers have shown that DR could be linked with overt or subclinical coronary disease as evidenced by Hallman, Aguilar, Piller LB, et al (87). Studies have made known that diabetics with retinopathy can have perfusion problems in myocardium, inferior coronary reserve, less coronary collaterals, increased calcification and extensive stenosis of arteries. It puts highlight on the fact that these microvascular and macrovascular complications might have common pathways and that cardiac disease might have a microvascular etiology other than the traditionally proposed macrovascular component.

"COMMON SOIL" HYPOTHESIS OF DIABETIC COMPLICATIONS

Experimental data have put forth that complications of micro and macrovasculature have similar pathophysiologies such as endothelial dysfunction function, inflammatory state, angiogenesis, programmed cell death and coagulation abnormalities.

Brownlee in his studies (88) has demonstrated that the sole basis for complications could be over zealous formation of superoxide radicals induced by hyperglycemia which in turn activates 4 gateways:

- polyol pathway
- hexosamine gateway
- protein kinase C (PKC) gateway
- AGE

Also insulin resistance produced by FFA causes augmented superoxide formation thus activating inflammatory state leading to impaired endothelial function.

ADVANCED GLYCATION END PRODUCTS

Chemical reactions among sugars and proteins yield advanced glycation end products. These have multiple effects like alteration of endothelium and collagen thickening. (89)

Specifically in retinopathy, it causes:

- apoptosis of pericytes in retina
- increased formation of VEGF,IGF-1,bFGF and HGF

- increase pathologic neovascularization
- Augment inflammation in vasculature.

Ultimately it causes endotheleial disturbance,thrombus formation and ischemia in retina. Angiogenesis, haemorrhage and finally fibrosis causes tractional retinal detachment and visual loss ensues. (90).

CVD PATHOGENESIS IN DIABETES

It has multifactorial causations; though, the common ground of injury is the endothelium. Diabetes first inhibits NO and blocks vasodilatation .Hyperglycemia itself inhibits the enzyme eNOS, augments the formation of reactive oxygen species tracking to furthermore inhibition of eNOS as a vicious cycle (91). Also the NO induced tissue plasminogen activator formation is impaired.Insulin resistance adds to this and also leads to increased FFA release from adipose and induces the ProteinKinase C pathway, which can again disrupt nitric oxide synthase activity through generation of reactive oxygen species. (72).

There is also an overproduction of vasoconstrictor substances such as endothelin 1, which mediates its effects either directly or through the renin angiotensin system.

Another common mechanism is a state of inflammation. These cells enter damaged endothelium and drift further deeper, imbibing LDL in oxidized state and thus resulting in foam cells, which are the basis of atherosclerosis. (62)

In conclusion, there are verifiable associations of DR with amplified risk of cardiovascular disease, independent of the established risk variables. More so, it may be that microvascular complications of diabetes manifest earlier than macrovascular complications. Therefore the benefits of treatments that reduce the risk for microvascular disease will ultimately reduce macrovascular disease as well. Thus patients having retinopathy concurrent with diabetes should undergo a thorough assessment of cardiac status periodically.

AIMS AND OBJECTIVES

1) To compare LV function by ECHO in Type 2 Diabetes mellitus patients with and without retinopathy.

2) To look for possible association between severity of DR and severity of cardiac dysfunction by ECHO, independent of possible confounding factors.

MATERIALS AND METHODOLOGY

Study Place : Department of General Medicine, Government Stanley Medical College & Hospital.

Study period : March 2012 to October 2012.

Study Design : Nested Case Control Study.

Sample size : 100 subjects.

INCLUSION CRITERIA:

Type 2 Diabetes mellitus patients attending Government Stanley Medical College and Hospital as Op/Ip.

EXCLUSION CRITERIA:

1) Previous history of cardiovascular disease.

2) Previous ocular diseases.

3) Concurrent medication with drugs altering cardiac dynamics.

Detailed history and thorough examination of the type 2 diabetes mellitus patients who were enrolled in the study were done. Fundus examination, retinopathy assessment and grading were done. ECHO was done and left ventricular function assessed. LV dysfunction in the study subjects in the presence or absence of retinopathy was compared.

The following data were collected from the patients.

Name :

Op/ Ip no :

Age :

Sex :

DIABETIC HISTORY: Age of onset, Duration.

CO MORBIDITIES: Hypertension, CVA, Nephropathy, Neuropathy, Diabetic foot, Peripheral vascular disease, Thyroid abnormalities, other endocrine abnormalities.

PERSONAL HISTORY: Smoking , Alcohol .

Blood pressure: reading of 140/90 mmHg was taken as hypertension.

Clinical assessment for CVA, peripheral vascular disease and neuropathy.

INVESTIGATIONS

- Blood sugar levels-fasting and post prandial
- HbA1C levels : levels>6.5% was taken as poor glycemic control.
- Renal function tests: Urea, Creatinine
- Urine-Albumin,Sugar,Deposits
- 24 hr urine proteinuria
- USG abdomen
- Fasting lipid profile: dyslipidemia was defined as a value of total cholesterol>200 mg/dl, TGL>150 mg/dl, HDL <40 mg/dl(men) and <50 mg/dl (women)
- Fasting thyroid function tests

- ECG
- Echocardiogram: 2D ECHO - to determine ejection fraction,mitral regurgitant jet volume calculation,E/A ratio calculation.
- Fundus examination: Done by ophthalmoscopy and subsequently slit lamp examination and fundus photography and graded as

  O - Normal

  1 - Background non proliferative

  2 - Preproliferative

  3 - Proliferative

  4 - Maculopathy

  5 – Post photocoagulation status

  6 - Unclassifiable.

STATISTICAL ANALYSIS

Data were collected in a preformed proforma. Statistical analysis was done using SPSS version 11.0 for Windows. Categorical data were expressed as absolute counts and percentages. Continuous data were expressed as mean and standard deviation.

For the variables in qualitative form, Chi square and Fisher's exact test was used in univariate analysis and further multivariate logistic regression was utilised to observe the association between the study variables and outcome. A p value of less than 0.05 was considered significant.

RESULTS AND OBSERVATIONS

A total of 100 subjects were included in the study. There were a total of 47 male patients and 53 female patients. A total of 42 subjects were aged above 60 years, the median age was 55.50 years with 95% C.I. being 53.2 to 57.5 years. Sixty five patients (65%) had a duration of diabetes for more than five years. Fifty eight patients (58%) among the study subjects had poor glycemic control.

Twenty four patients had comorbid hypertension, 39 patients had additional dyslipidemia. There were in total 18 subjects who gave history of smoking and 13 subjects with history of alcoholism.

Two of the study subjects had cerebrovascular accident, 3 had diabetic foot, 1 had peripheral vascular disease, 10 patients had diabetic nephropathy. In addition, two patients had co-existing thyroid disorders.

The incidence of diabetic retinopathy was 38% among the study population, and a total of 46% of study subjects had evidence of cardiac dysfunction. Twenty patients had systolic dysfunction, 43 patients had diastolic dysfunction and 17 patients had both. Thirty four of the study

subjects with LV dysfunction (LVD) had coexistent diabetic retinopathy (74%).

Table-1. Distribution of retinopathy among study population

TOTAL RETINOPATHY	38
BACKGROUND	23
PRE-PROLIFERATIVE	8
PROLIFERATIVE	3
MACULOPATHY	4

Table-2. Distribution of cardiac dysfunction among study population

TOTAL LVD	SD	DD GRADE 1	DD GRADE 2	DD GRADE 3	BOTH SD AND DD
46	20	33	7	3	17

A total of 26 patients who were more than 60 years had LV dysfunction in some form and the odds of patient >60 years to develop LV dysfunction was 3.0 compared to those less than 60 years, p value being <0.01. Forty patients among those with cardiac dysfunction (87%) had duration of diabetes more than five years and the odds of developing LV dysfunction for those with duration of diabetes more than five years was 7.73 compared to those with duration of diabetes less than five years, p value being significant ($p<0.05$).

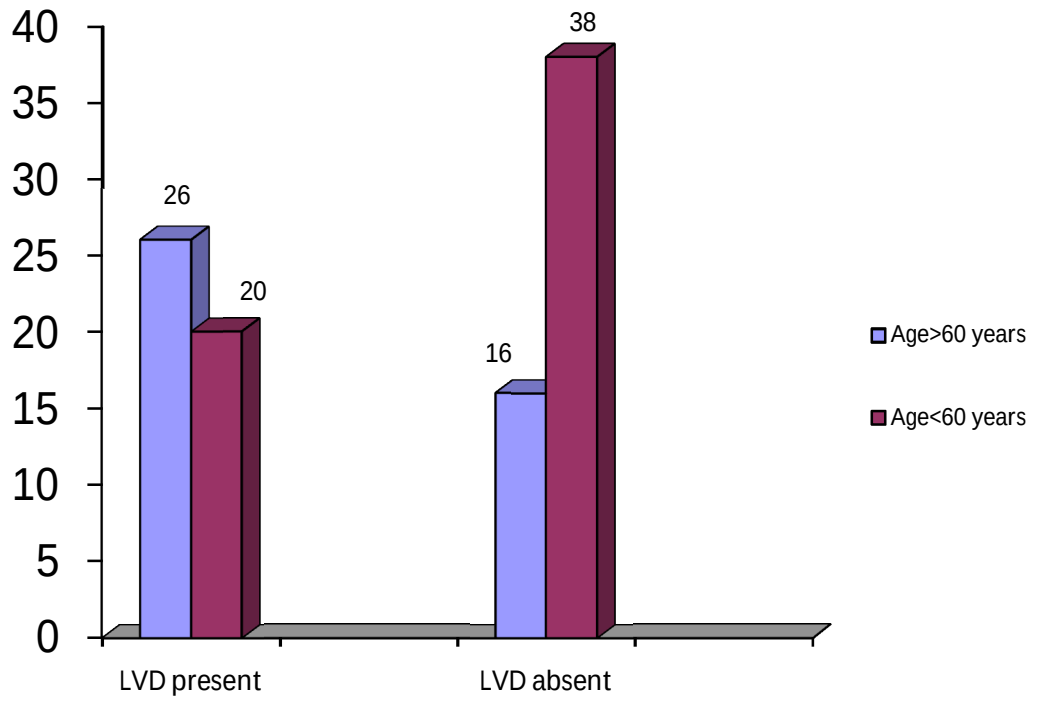
Table-3. Association of various factors with LVD in the study subjects

Factor	LVD Present n=46	LVD Absent n=54	Odds Ratio	95% C.I.	p value
Age>60 years	26	16	3.09	1.353-7.047	0.007
Male sex	23	25	1.160	0.528-2.550	0.712

DM Duration > 5 years	40	25	7.73	2.813-21.257	0.000
Poor glycemic control	29	29	1.471	0.659-3.282	0.346
Hypertension	13	11	1.540	0.612-3.873	0.357
Dyslipidemia	16	23	0.719	0.319-1.619	0.425
Smoking	7	11	0.702	0.247-1.989	0.504
Alcoholism	7	6	1.436	0.446-4.624	0.543
Nephropathy	6	4	1.875	0.427-8.610	0.349

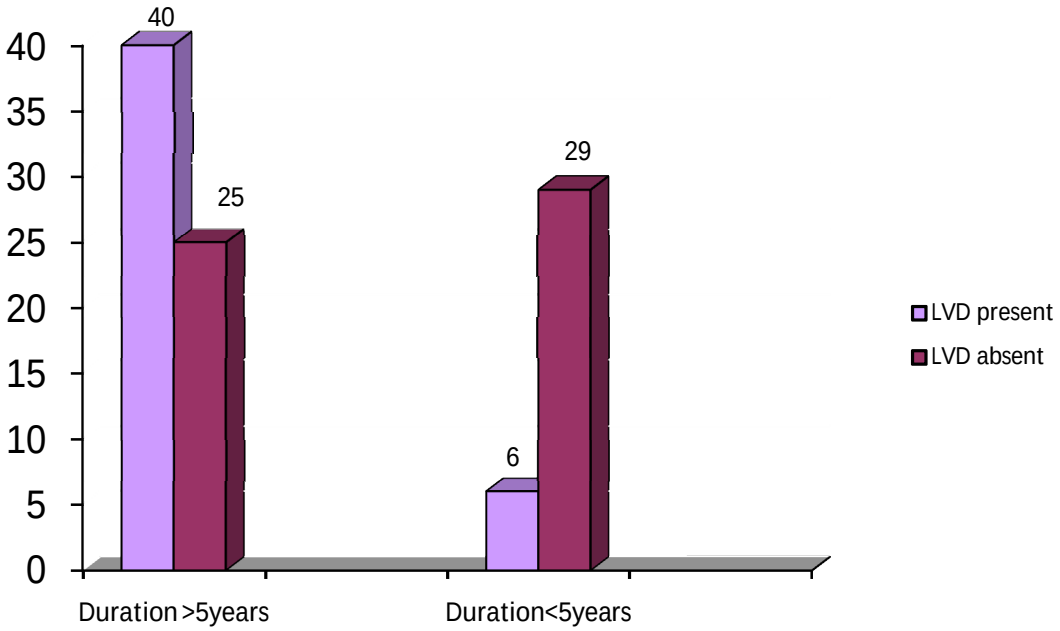
It is seen that age > 60 years and duration of diabetes more than 5 years were both significantly associated with LV dysfunction in the study subjects. Other factors such as gender, glycemic control, hypertension, dyslipidemia, smoking did not have any statistically significant association with the presence of cardiac dysfunction among the study subjects.

Fig-8. Age distribution of patients with LV dysfunction



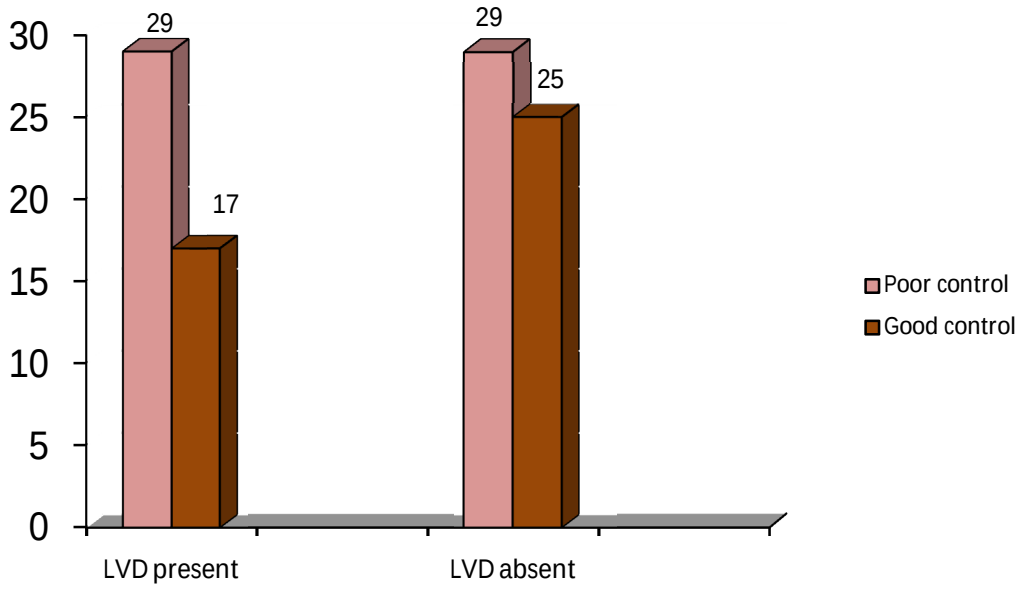
Among the patients with cardiac dysfunction, 26 patients (56.5%) were more than 60 years compared to 16 patients (29.6%) among those without cardiac dysfunction, which was statistically significant ($p<0.01$). There were 23 males (47.9%) and 23 females (44.2%), which was not statistically significant ($p=0.712$).

Fig-9. Diabetes duration in patients with cardiac dysfunction



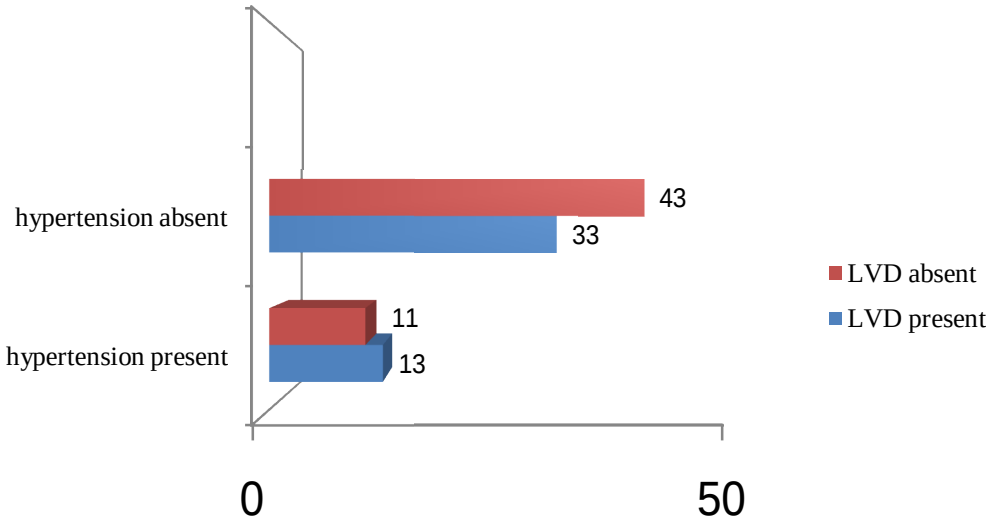
Among those with diabetes duration for more than five years, 40 patients(61.5%) had LV dysfunction compared to 25 patients(38.5%) who had no cardiac dysfunction, which was statistically significant ($p<0.05$). The odds of patients who are diabetic for more than 5 years are 7.73 to develop cardiac dysfunction compared to those who are diabetic for less than 5 years.

Fig-10. Glycemic control in patients with cardiac dysfunction



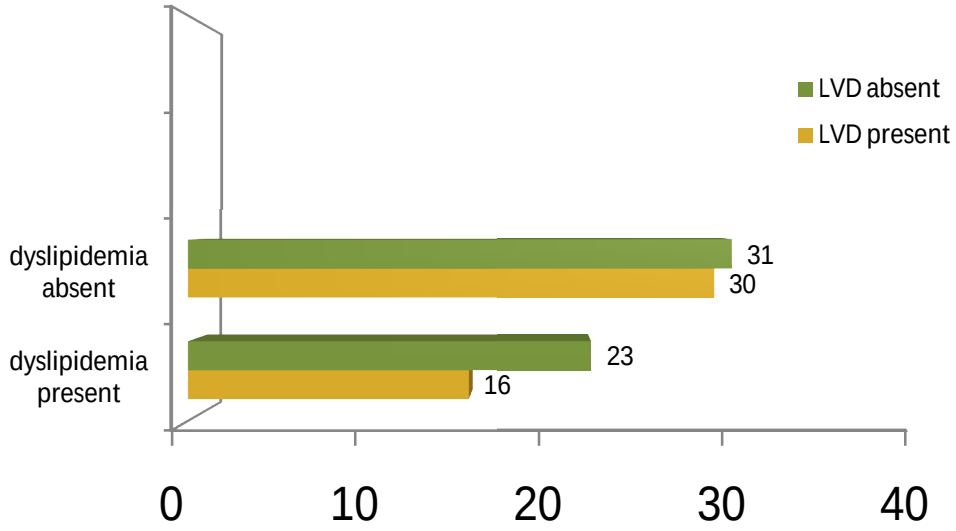
Out of 46 patients with LV dysfunction (LVD) 29 (63%) had poor glycemic control, compared to 17 (37%) with good glycemic control. The association was not statistically significant (p=0.34). Other factors such as smoking, alcoholism also did not have a significant association with cardiac dysfunction.

Fig-11. Hypertension in patients with LV dysfunction



The presence of hypertension did not have statistically significant association with the development of LV dysfunction (p=0.357).

Fig-12. Dyslipidemia in patients with LV dysfunction



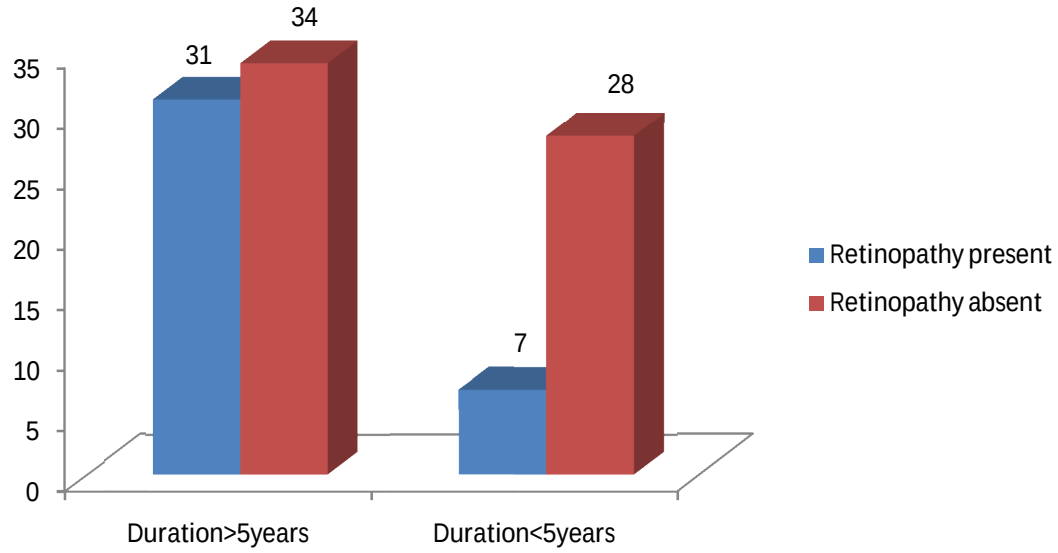
The presence of dyslipidemia did not have statistically significant association with the development of LV dysfunction (p=0.425).

Table-4. Multivariate logistic regression for variables associated with LV dysfunction

Variable	Standard Error	Adjusted Odds Ratio	95% C.I	P Value
Diabetic Retinopathy present	0.72	40.08	9.84-163.25	p<0.001
Diabetes Mellitus Duration >5 years	0.75	7.41	1.70-32.3	p<0.01

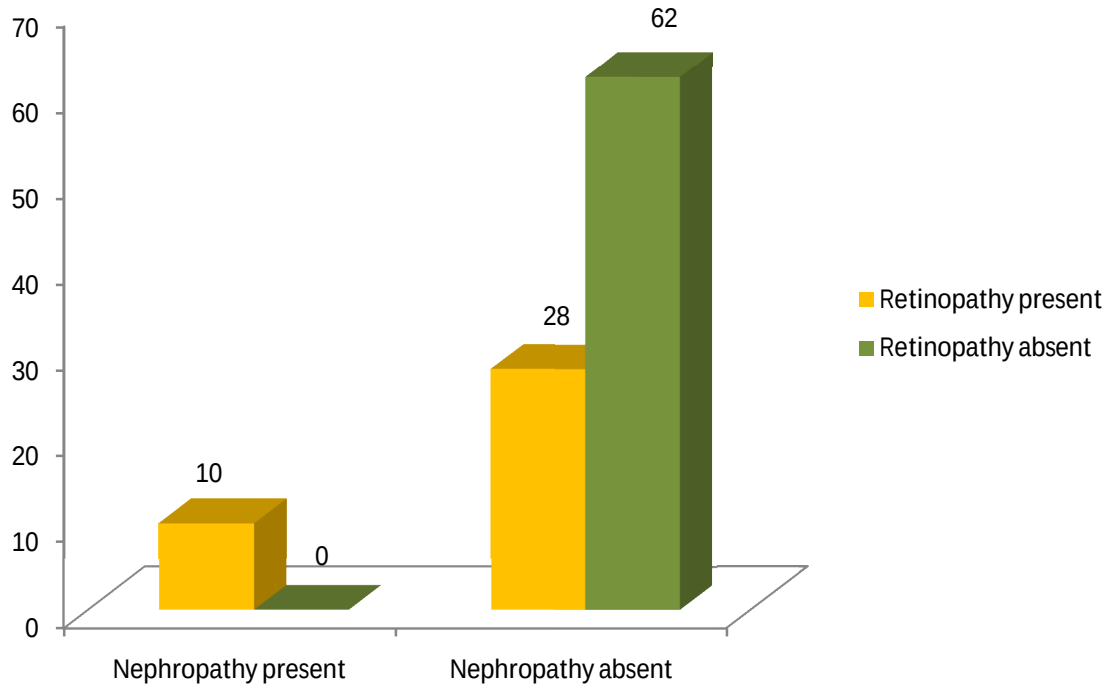
Multivariate analysis revealed that presence of diabetic retinopathy and duration of diabetes more than 5 years were independently associated with LV dysfunction in the study subjects.

Fig-13. Diabetes duration in patients with retinopathy



A total of 31 patients (91.2%) who had duration of diabetes more than 5 years also had retinopathy, compared to a total of 7 patients (25%) with disease duration of less than 5 years who developed retinopathy as a complication.

Fig-14. Nephropathy in patients with retinopathy



Among the study subjects, a total of 10 patients had evidence of nephropathy, all of whom also had concomitant retinopathy.

Table - 5. Association of various factors with retinopathy in the study subjects

Factor	Diabetic retinopathy present n=38	Diabetic retinopathy absent n=62	Odds ratio	95% C.I.	p value
Age > 60 years	19	23	1.69	0.69-4.17	0.20
DM duration > 5 yrs	31	34	3.64	1.28-10.72	0.007
Poor glycemic control	22	36	0.99	0.40-2.44	0.98
Hypertension	7	17	0.59	0.19-1.77	0.30
Dyslipidemia	17	22	1.47	0.59-3.64	0.35
Nephropathy	10	0			0.00

Univariate analysis of various factors associated with retinopathy revealed that duration of diabetes more than 5 years and presence of diabetic nephropathy had statistically significant association with the development of retinopathy.

Other factors such as age, gender, glycemic control, hypertension, dyslipidemia, smoking, alcoholism did not have statistically significant association with presence of diabetic retinopathy.

Fig-15. LV dysfunction in patients with diabetic retinopathy

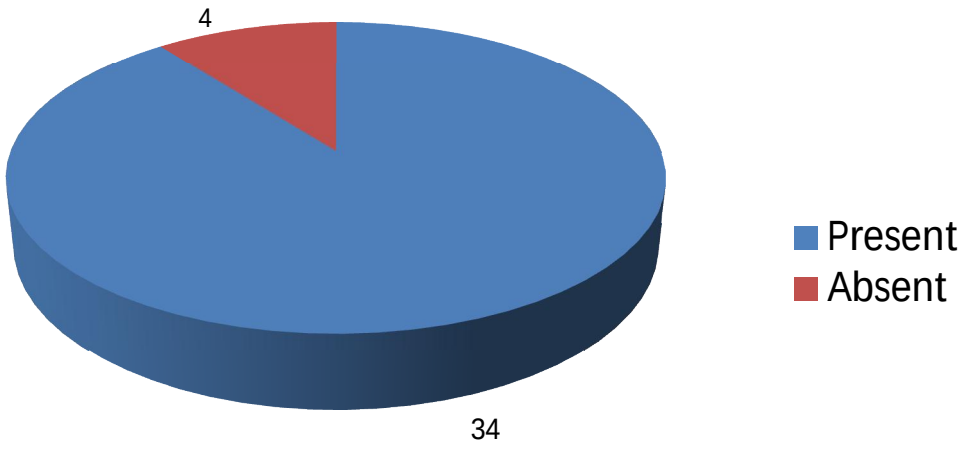
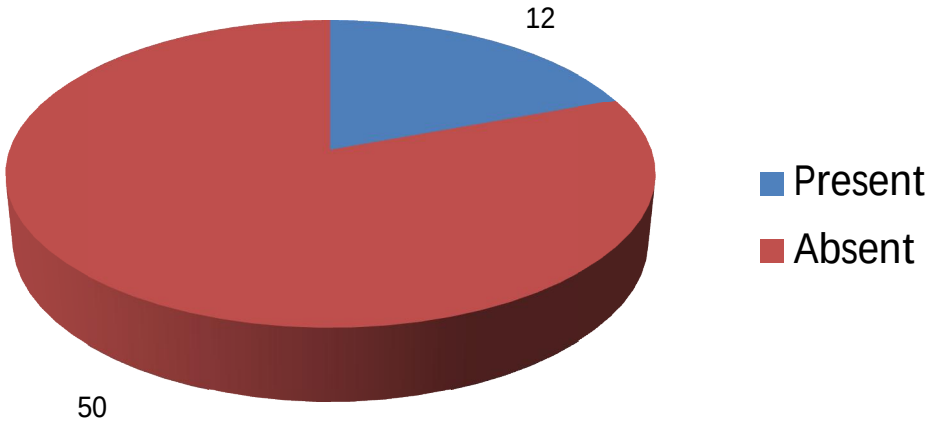
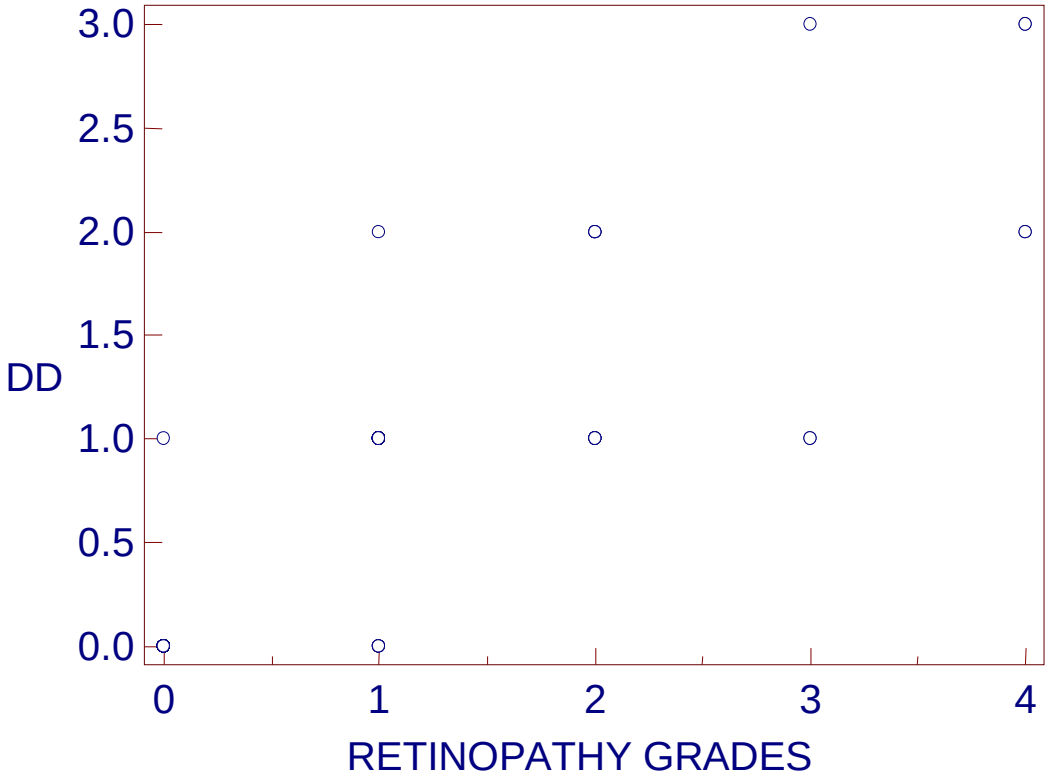


Fig-16. LV Dysfunction in patients without diabetic retinopathy



It was observed that 89.5% of patients with diabetic retinopathy had LV dysfunction compared to 19.4% patients among those without diabetic retinopathy, and the p value was significant ($p<0.001$) as evaluated by Fisher's exact test.

Fig-17. Scatter diagram showing correlation of grades of Retinopathy and Diastolic dysfunction



From the above scatter plot, it is evident that a strong positive correlation exists between the grades of Retinopathy and grades of Diastolic Dysfunction (DD) and is found to be significant (Correlation co-efficient =0.897; C.I.= 0.85-0.92, $p<0.0001$).

Fig -18. Age distribution among patients with cardiac dysfunction with and without retinopathy

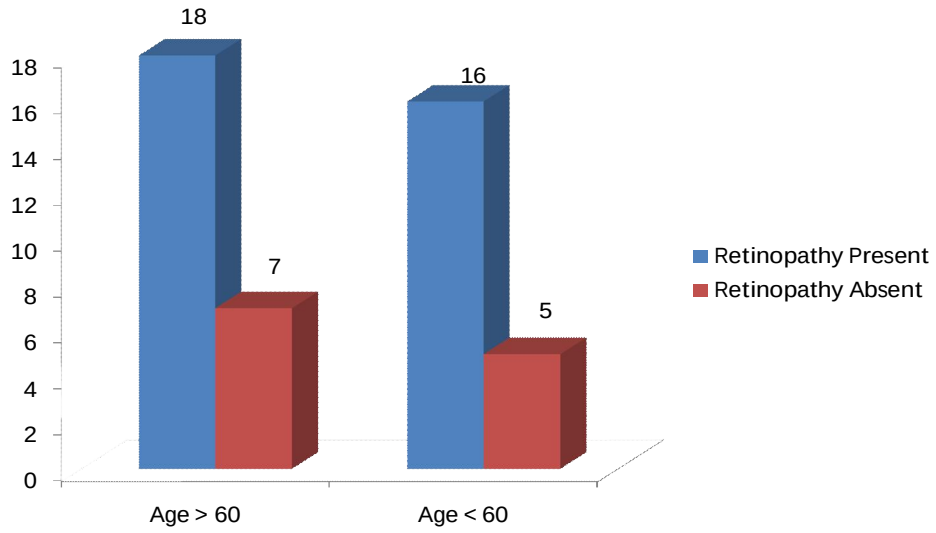


Fig-19. Sex distribution among patients with cardiac dysfunction with and without retinopathy

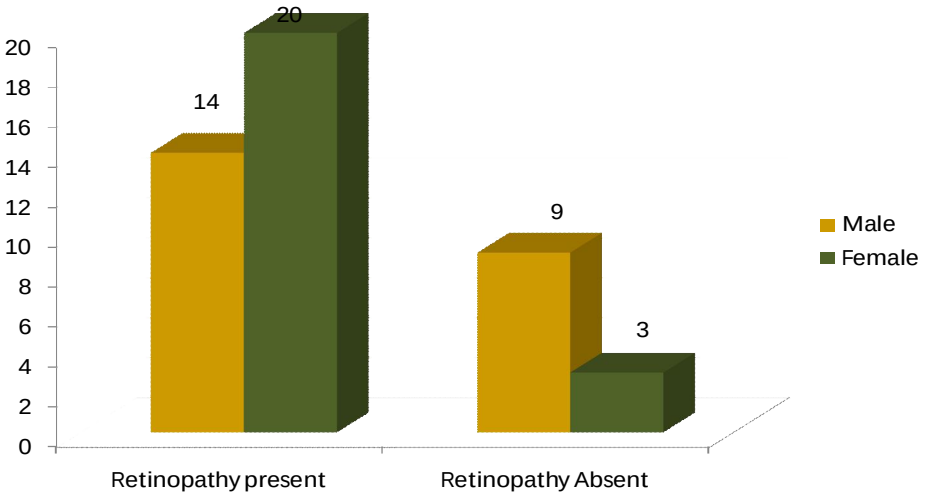


Fig-20. Duration of diabetes mellitus among the patients with cardiac dysfunction

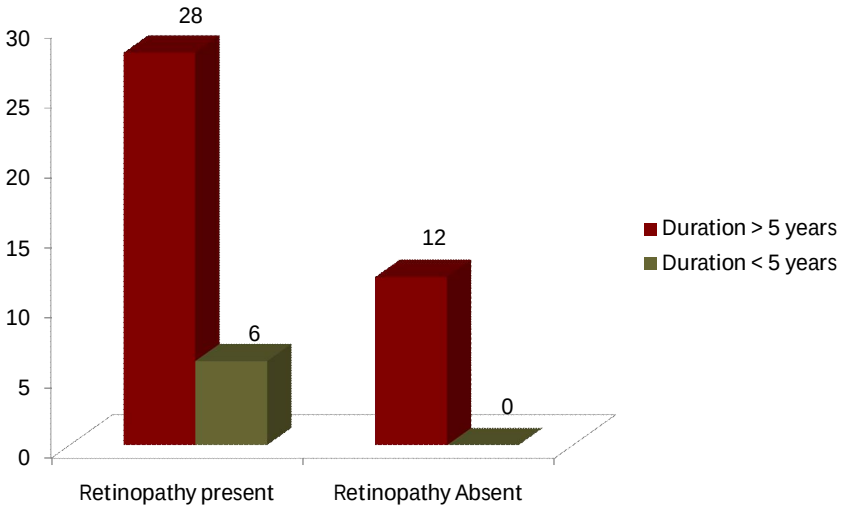


Fig-21. Glycemic control among patients with cardiac dysfunction

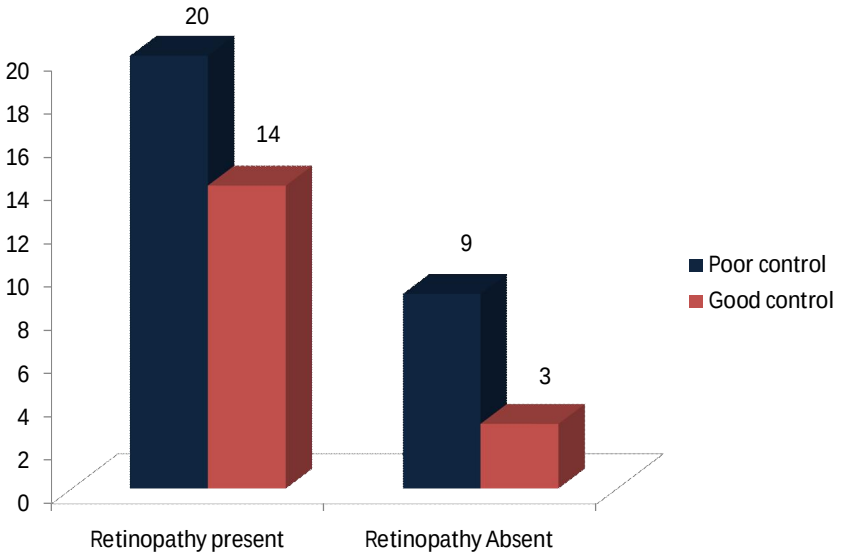
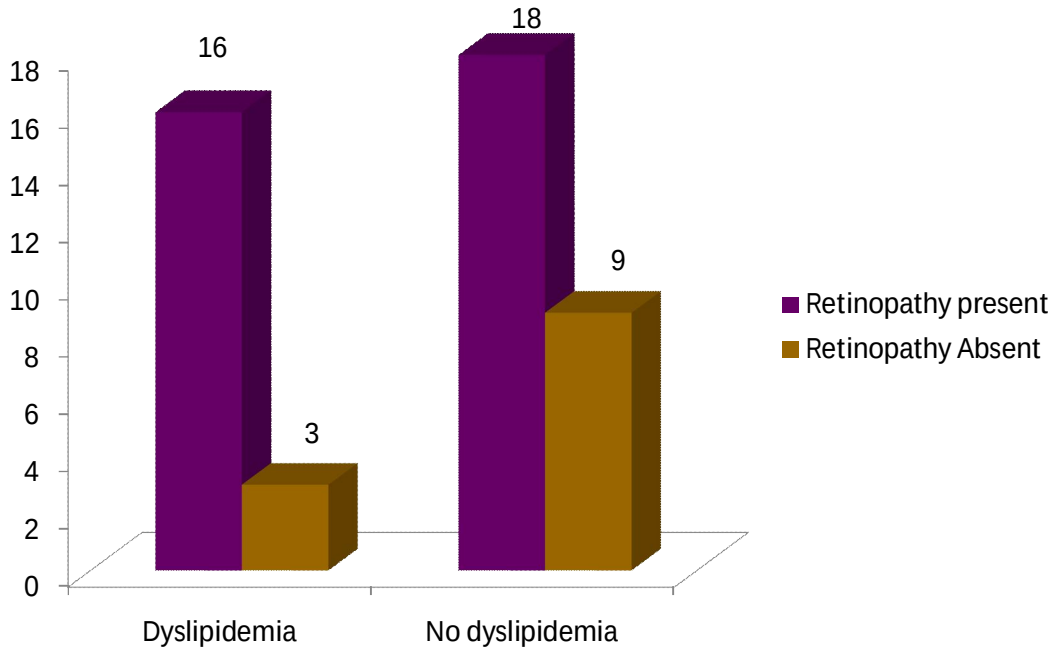


Fig-22. Dyslipidemia among the study subjects with cardiac dysfunction



There was no statistically significant difference between the two groups with respect to the presence or absence of dyslipidemia.

Table-6. Comparison between patients with and without retinopathy who developed LV dysfunction

Variable	No. of patients with retinopathy	No. of patients without retinopathy	P value	Odds ratio	95% C.I.
Age > 60	18/34	7/12	0.747	0.804	0.174-3.643
Diabetes duration > 5 years	28/34	12/12	0.119	0	0-2.639
Poor glycemic control	20/34	9/12	0.318	0.476	0.083-2.470
Hypertension	7/34	6/12	0.05	0.259	0.005-1.287
Dyslipidemia	16/34	3/12	0.182	2.667	0.518-15.203

Factors such as age, gender, duration of diabetes, glycemic control, hypertension, dyslipidemia did not differ significantly between those with and without retinopathy who developed cardiac dysfunction.

DISCUSSION

A total of 100 diabetic patients were included in the study, and cardiac function was assessed by 2D and Colour Doppler echocardiography. The study subjects included patients with type 2 diabetes mellitus. Previous studies which analysed cardiac function in diabetic subjects included type 1 diabetes as in studies by Sampson et al (82), Perez et al (39), while similar study was done in type 2 diabetes patients by Annonu et al (41).

A total of 46 patients had LV dysfunction (LVD), among which 20 had systolic dysfunction, 33 had diastolic dysfunction and 17 had both systolic and diastolic dysfunction. Historically, cardiac dysfunction was assessed by cardiac catheterization (92) and later non-invasive methods were employed which included irregular time intervals by using phonocardiograms, assessment of ventricular filling by standard ECHO (93), as well as Doppler ECHO.

Diastolic dysfunction was more prevalent than systolic dysfunction which was similar to the observations by Raev et al (94). The subjects included in the study by Raev et al included Type 1 Diabetes mellitus

patients. In the study by Cosson et al, 69% of the subjects had cardiac dysfunction (95), compared to our study where 46% had cardiac dysfunction. This could be explained by the technical limitations in echocardiography.

There were totally 38 patients with retinopathy and the distribution of retinopathy was as follows: 23 (60.5%) had background retinopathy, 8 (21%) had pre-proliferative retinopathy, 3 (8%) had proliferative retinopathy and 4 (10.5%) had diabetic maculopathy. There were no significant differences between age, sex, dyslipidemia, glycemic control, dyslipidemia and hypertension.

However, significant association was found between presence of diabetic nephropathy and duration of diabetes more than 5 years. A study by Aguilar et al revealed noteworthy dissimilarities in sex, smoking and lipid profile between the two groups. Also more severe grade of retinopathy was linked with hypertension, prolonged diabetes duration and albuminuria in that study (87).

A more severe grade of retinopathy was coupled with higher grades of cardiac dysfunction which was similar to the observations made by Aguilar et al (87). However, studies by Airaksinen et al (42) and Uusitupa et al (43) did not find any significant association with cardiac dysfunction and presence or absence of retinopathy.

Multivariate analysis revealed that presence of retinopathy and duration of diabetes more than five years had significant association with the development of LV dysfunction in the study subjects. The results are similar to the study done by Virendra et al, where diabetic patients with retinopathy had higher incidence of LV diastolic dysfunction and it correlated with the duration of diabetes mellitus in the study subjects (96).

CONCLUSIONS

Type 2 Diabetes mellitus patients with diabetic retinopathy had significant association with impaired LV function detected by echocardiography in comparison to those without retinopathy. The severity of retinopathy in these patients correlated with grade of diastolic dysfunction.

Diabetic patients who are detected with retinopathy should also be assessed for asymptomatic cardiac involvement. However, there must be studies with a larger sample size and follow up period to know the natural history of cardiac involvement in patients with type 2 diabetes mellitus and trials to study the benefit for cardiac screening in such individuals, before strong recommendations are made.

ANNEXURES

PROFORMA

PATIENT DETAILS

- Name:
- OP/ Ip no:
- Age:
- Sex:
- Occupation:
- Address:
- DIABETIC HISTORY

    Age of onset:

    Duration:

- Mode of treatment:

    1. Oral hypoglycemic agents
    2. Insulin

- COMORBIDITIES:

  HT/CVA/Nephropathy/Neuropathy/DF/PVD/Thyroid/Other Endocrine Abnormalities

- PERSONAL HISTORY : Diet ,Smoking ,Alcohol

- FAMILY HISTORY

EXAMINATION

- General examination

- BMI

- BP

- Cardiovascular system examination

- Respiratory system examination

- Per abdominal examination

- Nervous system examination: Higher motor functions, Cranial nerves, Motor system, Sensory system.

- FUNDUS

INVESTIGATIONS

- Blood sugar-Fasting blood sugar, Post prandial blood sugar.
- HbA1c levels.
- Renal function test-Urea, Creatinine.
- Urine-Albumin, Sugar, Deposits.
- 24 hr urine proteinuria
- Fasting lipid profile
- Fasting Thyroid function tests
- USG abdomen
- ECG
- Echocardiogram

ABBREVIATIONS

- DM-diabetes mellitus
- DM DUR-diabetes mellitus duration
- POOR GC-poor glycemic control
- DR-diabetic retinopathy
- LV-left ventricle
- LVD-left ventricular dysfunction
- LVH-left ventricular hypertrophy
- CVD-cardiovascular disease
- CAD-coronary artery disease
- CVA-cerebrovascular accident
- ECG-electrocardiogram
- ECHO-echocardiogram
- HT-hypertension
- DL-dyslipidemia
- SMO-smoking
- ALC-alcohol
- PVD-peripheral vascular disease
- DF-diabetic foot
- THY-thyroid
- ENDO-endocrine disorders

- NEP-nephropathy
- NEU-neuropathy
- G.RE-grading of retinopathy
- SD-systolic dysfunction
- DD-diastolic dysfunction
- RET-retinopathy
- MRI-magnetic resonance imaging
- OHA-oral hypoglycemic agents
- GDM-gestational diabetes mellitus
- PCOS-polycystic ovarian syndrome
- DKA-diabetic ketoacidosis
- BMI-body mass index
- BP-blood pressure
- IRMA-intraretinal microvascular abnormalities
- NVD-new vessels on the disc
- NVE-new vessels elsewhere
- WESDR- Wisconsin Epidemiologic Study of Diabetic Retinopathy
- CURES-chennai urban rural epidemiological study
- DCCT- Diabetes Control and Complications Trial
- UKPDS-united kingdom prospective Diabetes study
- VEGF-vascular endothelial growth factor

- GH-growth hormone
- TGF-transforming growth factor
- CSME-clinically significant macular edema
- AGE-advanced glycation end products.
- MI-myocardial infarction
- FFA-free fatty acid
- IGF-insulin like growth factor
- HGF-hepatocyte growth factor
- FGF-fibroblast growth factor
- NO-nitric oxide
- eNOS-endothelial nitric oxide synthase.

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MASTER CHART

S No	NAME	IP/OP NO	AGE	SEX	DM DUR	POOR GC	HT	DL	SMO	ALC	CVA	PVD	DF	THY	ENDO	NEP	NEU	G. RET	SD	DD	RET	LVD
1	ulaganathan	38162	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	kumar	38065	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
3	krishnaveni	3901	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	selvan	37146	1	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
5	revathy	4397	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	3	1	1	1	1
6	arumugam	35294	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1
7	jayaraman	36289	1	1	1	0	1	0	1	0	0	0	0	1	1	0	0	0	0	0	0	0
8	devika	30832	0	0	1	0	0	1	0	0	0	0	0	0	0	1	0	4	1	2	1	1
9	mary	43835	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	aruldoss	35144	0	1	1	1	0	0	0	0	0	0	0	0	0	1	0	0	1	1	0	1
11	rathnamal	81479	1	0	1	1	1	0	0	0	0	0	0	0	0	0	0	4	1	2	1	1
12	prem kumar	31644	0	1	1	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
13	kamala	20224	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14	periyasamy	23560	1	1	1	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	1
15	latha	43845	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16	sharada	30284	1	0	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0	1	1	1
17	jothi	43096	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1
18	musthafa	32640	1	1	1	0	1	1	0	0	0	0	0	0	0	1	0	0	1	1	0	1
19	kala	53916	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20	sujatha	30159	0	0	1	1	0	1	0	0	0	0	0	0	0	1	0	3	1	1	1	1
21	ganesan	5277	0	1	0	0	1	1	0	0	0	0	0	0	0	0	0	1	0	1	1	1
22	maniyamal	42773	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1

S No	NAME	IP/OP NO	AGE	SEX	DM DUR	POOR GC	HT	DL	SMO	ALC	CVA	PVD	DF	THY	ENDO	NEP	NEU	G. RET	SD	DD	RET	LVD
23	kalyani	29969	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	2	0	1	1	1
24	jaya	42068	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1
25	mani	40752	1	1	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
26	lakshmi	42069	1	0	1	1	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	1
27	iqbal	31698	1	1	1	1	0	0	0	1	0	0	0	0	0	1	0	2	0	2	1	1
28	rajeshwari	42054	1	0	1	1	0	1	0	0	0	0	0	0	0	1	0	1	1	1	1	1
29	kannan	30734	1	1	1	1	0	1	0	0	0	0	0	0	0	0	0	1	0	1	1	1
30	edwin	30719	0	1	1	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
31	vasantha	41995	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
32	elumalai	27574	1	1	1	0	0	0	1	1	0	0	1	0	0	0	0	1	0	1	1	1
33	rani	41971	0	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
34	krishnan	27548	0	1	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
35	komala	41058	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1
36	samuel	25575	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
37	elizabeth	40045	0	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
38	pitchumani	32642	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	2	0	1	1	1
39	sathya	39237	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	1	0	1	1	1
40	ibrahim	43398	0	1	1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
41	mahalingamal	48615	0	0	1	0	0	1	1	0	0	0	0	0	0	0	0	4	1	3	1	1
42	thilagam	39101	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	1	0
43	minnala	263454	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0
44	kannan	41942	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
45	kaliamal	37142	1	0	1	1	0	1	0	1	0	0	0	0	0	0	0	2	1	1	1	1
46	amaravathy	37176	1	0	0	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
47	kaliyappan	42010	0	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1

S No	NAME	IP/OP NO	AGE	SEX	DM DUR	POOR GC	HT	DL	SMO	ALC	CVA	PVD	DF	THY	ENDO	NEP	NEU	G. RET	SD	DD	RET	LVD
48	francis	42722	1	1	1	1	1	0	0	1	0	0	0	0	0	1	0	0	1	0	0	1
49	govindaraj	42766	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50	pushpa	24644	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
51	thanayan	42756	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
52	shanmugam	39080	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
53	ramalingam	40058	1	1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
54	alangaram	36290	1	0	1	1	0	1	0	0	0	0	0	0	0	0	0	1	0	1	1	1
55	rajan	41005	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
56	mannangati	41067	1	1	1	1	1	0	0	0	0	0	0	0	0	1	0	2	0	1	1	1
57	muniyamal	39021	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
58	baskaran	43026	0	1	0	1	0	1	1	0	0	0	0	1	1	0	0	2	0	2	1	1
59	viji	42316	0	1	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
60	rathiamal	42737	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
61	mathialagan	41055	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	2	1	2	1	1
62	mohanavalli	36253	1	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
63	muthulakshmi	36223	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
64	moorthy	40851	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1
65	devendran	40285	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
66	vijayalakshmi	36241	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
67	mubarakbasha	40281	0	1	0	1	0	1	0	0	0	0	0	0	0	0	0	1	0	1	1	1
68	mary	35210	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1
69	kamala	35242	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
70	sivakumar	40238	0	1	0	0	0	0	1	1	0	1	1	0	0	0	0	0	0	0	0	0
71	subramani	39367	0	1	1	1	0	1	1	0	0	0	1	0	0	0	0	1	0	1	1	1
72	kanmani	34441	1	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1

S No	NAME	IP/OP NO	AGE	SEX	DM DUR	POOR GC	HT	DL	SMO	ALC	CVA	PVD	DF	THY	ENDO	NEP	NEU	G. RET	SD	DD	RET	LVD
73	govindammal	34436	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
74	selvaraj	39318	1	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
75	gowri	33558	1	0	0	1	0	1	0	0	0	0	0	0	0	0	0	1	0	1	1	1
76	durai	39305	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0
77	perundevi	32636	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
78	neeladevi	31878	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
79	rathnavel	39277	0	1	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0	1	1	1
80	shakunthala	31625	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
81	jayalakshmi	31746	1	0	1	0	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	1
82	sekar	39275	0	1	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
83	veeraraghavan	42335	0	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
84	padma	29248	1	0	1	1	1	1	0	0	0	0	0	0	0	0	0	2	1	2	1	1
85	raniamal	28635	1	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
86	isrel	38433	0	1	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
87	devanayaki	26610	1	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
88	gnanakumari	26593	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
89	amanullah	36497	1	1	0	1	1	0	0	0	0	0	0	0	0	0	0	3	1	3	1	1
90	sathya	25502	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
91	vasantha	24658	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
92	pushpavalli	24644	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
93	moorthy	36534	0	1	1	1	1	0	1	1	0	0	0	0	0	0	0	4	1	3	1	1
94	elumalai	35459	0	1	0	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
95	rukmani	23732	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
96	selvambal	21052	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	2	1	1
97	lakshmi	20927	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0

S No	NAME	IP/OP NO	AGE	SEX	DM DUR	POOR GC	HT	DL	SMO	ALC	CVA	PVD	DF	THY	ENDO	NEP	NEU	G. RET	SD	DD	RET	LVD
98	sumathy	20019	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
99	muthukrishnan	42324	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
100	chinaiyah	38331	0	1	1	0	0	1	1	1	0	0	0	0	0	0	0	0	1	1	0	1

KEY

1. NAME

2. AGE: below 60-0, Above 60-1

3. SEX: Male -1, Female – 0

4. IP/OP NUMBER

5. DM DUR-diabetes mellitus duration: <5 yrs -0, >5 yrs-1

6. POOR GC- poor glycemic control: Absent – 0,present – 1

7. HT- hypertension: Absent – 0, present – 1

8. DL-dyslipedemia : Absent – 0,present – 1

9. SMO- smoking: Absent– 0, present – 1

10. ALC- alcoholism: Absent – 0, present 1

11. CVA- cerebrovascular accident : Absent – 0, present – 1

12. PVD- peripheral vascular disease: Absent – 0, present – 1

14. DF- diabetic foot : Absent – 0, present – 1

15. THY- thyroid abnormalities: Absent – 0, present – 1

16. ENDO-other endocrine abnormalities: Absent – 0, present – 1

17. NEP-nephropathy: Absent – 0, present – 1

18. NEU-neuropathy: Absent – 0, present – 1

19. G.RET-retinopathy with grading:

    Nil -0

    Background retinopathy-1

    Pre-proliferative -2

    Proliferative -3

    Maculopathy-4

    Photocoagulation-5

    Unclassifiable-6

20. SD- systolic dysfunction: absent 0, present 1

21. DD- diastolic dysfunction: Absent – 0, Grade 1 – 1, Grade 2 – 2, Grade 3 – 3

22. RET- retinopathy in toto - Absent-0, Present-1

23. LVD-left ventricular dysfunction on the whole: Absent-0, Present-1

INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Comparative study of left Ventricular function by Echocardiography in type 2 diabetes mellitus patients With or without Retinopathy

Principal Investigator : Dr.K.Bhargavi

Designation : PG in M.D(Gen.Med)

Department : Department of General Medicine
Government Stanley Medical College,
Chennai-1

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 06.03.2012 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

04/10/12

MEMBER SECRETARY,
IEC, SMC, CHENNAI